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EXHIBIT A

**S & THORNBURG** 

P.O. Box 2786 Chicago, Illinois 60690-2786 (312) 357-1313 (312) 759-5646 Fax

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

I hereby certify that this correspondence is being Group: 1641 deposited with the United States Postal Service as Express Mail No. EL 99003872 US in an envelope Confirmation No.: addressed to Commissioner for Patents, P.O. Box 1450. Alexandria, VA 22313-1450 Application No.: 09/848,967 on July , 2004 Invention: IMMUNOGENIC PEPTIDES AND USES THEREOF Alice O. Martin Registration No. 35,601 Emanuel Calenoff and Charles Ditlow Applicant: Filed: May 4, 2001 Attorney Docket: 21417/92378 CHEU, CHANGHWA J Examiner:

#### **DECLARATION UNDER 37 C.F.R. § 1.132**

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

I, Byron Anderson, have read the patent application captioned above. A copy of my curriculum vitae is appended to indicate my expertise in the area of the invention described therein.

I have approximately 39 years of research experience in protein and peptide structures, immunochemistry and antibody responses. I recently retired from a faculty position at the Medical School of Northwestern University after 32 years of service. I taught for all those years the subjects of protein structure and peptide chemistry, and immunochemistry, including the subjects of antibody binding to epitopes and what constitutes an epitope of various chemical natures. I am now employed as a consultant to two companies on the subjects: peptide immunogens for eliciting antibodies with

selective reactivities to an alcoholic related form of the transferrin glycoprotein (this is the subject of a patent of which I am a co-inventor as listed on my CV), and a peptide library of D-aromatic rich peptides that show high affinites for various proteins of clinical interest (a patent application has been filed on this subject with myself as sole inventor as listed on the CV). We have also published papers and filed patent applications on the subjects: (1) production of antibodies to a N-terminal sequence of a connective tissue activating protein, (2) a peptide sequence which binds immune complexes, (3) antibodies to a reduced Glc-peptide of the N-terminus of glycated-hemoglobin which selectively binds such protein, and (4) a peptide sequence prediction algorithm for carbohydrate binding sites of proteins.

With this background I feel I can comment knowledgeably about the Calenoff – Ditlow patent application and the patent examiner's discussion.

- 1. I have no relationship to the patent application captioned above, and will not benefit financially from its commercial development.
- 2. In my review of the documents sent to me, I first read the review paper by Regenmortel, Mark H.V. (1998) ASM News/vol. 64, no. 6, pp. 332-338, then the Calenoff Ditlow patent application, followed by the patent examiner's comments in the Office Action mailed May 17, 2004.
  - 3. I understand that the examiner believes that several publications, in particular Regenmentel, teach the same things as the present invention, or make it obvious.
  - 4. I will first describe the major elements of the Regenmortel paper and comment here and later on the relationship to the examiner's comments and the patent application as follows:
    - a. The Regenmortel paper (the paper) first explains what is generally accepted as definitions for epitopes of peptide chemical nature (continuous or discontinuous), and for paratopes (those portions of a receptor, for example, the antibody combining site regions), for epitope-paratope non-covalent binding interactions which define specificities and affinities, and why a peptide of dissimilar sequence from the epitope peptide sequence may bind into the same paratope regions via a summation of different atomic non-covalent bondings or by the use of other sub-regions within the paratope regions. The paper also describes mimotopes: Mimotopes are peptides

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usually identified from combinatorial peptide libraries which functionally mimic the epitope, ie, by binding with some defined affinity to the same receptor as the epitope (in the cases cited, binding to antibody combining sites). The sequence of the peptide mimotope may have some sequence similarity to the epitope or may have no sequence homology, the specific non-covalent bonding interactions of mimotope peptide to the paratope regions having some similarities or being very dissimilar to those of the epitope bondings. At this point it should be noted that mimotopes are not proteins, or peptide sequences derived from proteins, and mimotopes cannot be defined as a comparative protein as the examiner has done in his comments on the patent application.

In Figure 4, Regenmortel shows some viral protein peptide sequences and 4 mimotopes that show various amounts of homologies. The reason there are homologies of the mimotopes to the viral peptide sequences is: Peptide libraries are generated by phage tail protein displays of randomized sequences of peptides at the N-terminus of the tail protein, or the libraries are chemically synthesized on beads (Tenta-Gel beads are those preferred) by an addition – mix process. Such libraries (if all 20 different amino acids are used) should contain all possible peptide sequences of the length chosen (eg, hexapeptides). Therefore, within the library one should find both the exact sequence of an epitope of equal length as well as many peptides of sequence homology. Thus, the libraries of mimotopes will contain some number of peptide sequences that will functionally mimic an epitope and exhibit such homologies.

Regenmortel then has a short description of the prediction of viral antigens: surface accessibility of such peptide sequences and N- or C-terminal locations (by well known algorithms and as used by Calenoff-Ditlow), and mentions using overlapping peptide sequence analyses to empirically discover reactive peptides.

b. The Calenoff-Ditlow application describes methods for identifying epitopes of proteins of interest: A selection of proteins (the target proteins) of a microorganism or other protein associated with a disease state is first made. Then published algorithms are used to ascertain which peptide regions are more likely to be exposed on the protein surface and thus accessible for binding with antibody reagents. Then follows

the unique and inventive steps of Calenoff-Ditlow: The protein surface probable sequences (the PSP sequences) are compared to all other known proteins (comparative proteins) for possible sequence homologies and those which are less than 50% homologous to sequences of other proteins, and which have less than 4 or more contiguous amino acids identical to the comparative protein sequences, are selected for use as immunogens and are the peptides for which composition claims are made. The resulting antibody reagents are then tested for reactivities to antigens in sera of persons with particular disease states related to the initial selected (target) protein(s), and compared to reactivities of sera of a control group. Obviously, those reacting with antigens in the particular disease state and not with controls can then be studied for utility as diagnostic reagents or as therapeutic agents. Examples are given and the data therein clearly support the invention idea and the utility. The invention, in my opinion, is consistent with the claims: peptide sequences of particular utility and the compositions of those selected and tested peptides.

c. The examiner states (under number 102) that Regenmortel teaches the method of identifying peptide epitopes using in the first steps the algorithm prediction programs. This is fine and is also used by Calenoff-Ditlow as discussed above. The examiner then says that Regenmortel teaches the functional, and to varying degrees the sequence homologies, of mimotopes. The examiner then equates the mimotope peptide (number 13) to a peptide sequence selected by the method of Calenoff-Ditlow because of points (a) through (f) as listed by the examiner.

Reasons why this is not a correct interpretation or correlation to the Calenoff-Ditlow method:

The mimotope is not derived from the protein HbsAg sequence 120-132 as the examiner states (point b), therefore no predetermined link exists between the mimotope sequence and the target protein. Rather, the mimotope is derived from the peptide library and may have certain sequence homology to the HbsAg sequence for the reasons discussed above. However, the mimotope is an entirely different entity from either the target protein or the comparative proteins, or the peptides described in Calenoff-Ditlow. Thus it is incorrect to assign any equivalence of fact or inference.

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- A mimotope is not an immunogenic peptide equivalent to those used by Calenoff-Ditlow. Immunogenic means that the peptide has been demonstrated to elicit an immunologic response, cell-mediated or antibody. Again, the mimotopes are derived from a peptide library and were not used as immunogens in the examples of the Regenmortel paper. In Calenoff-Ditlow, the identified peptide sequences of the target proteins are used as immunogens.
- The HCV protein of Figure 4 of Regenmortel could be used as a comparative protein as the examiner states. However, the examiner has taken this example out of the context of the Regenmortel paper, and as would be generally used by immunologists (and as used by Calenoff-Ditlow). It is true that the HCV sequence 20-32 shows no homology to the HbsAg sequence 120-132 as the examiner states. However, as used by Regenmortel, this is simply an additional example of a protein antigenic sequence for which a mimotope was identified, ie, the mimotope P551c. In contrast, parts of the invention steps of Calenoff-Ditlow are to compare the PSP sequences to all other known protein sequences and then to select those PSP sequences of less than 50% homology and less than 4 contiguous amino acid sequences. This is quite different and bears no relationship to the fact that the various peptide sequences in Figure 4 of Regenmortel do not exhibit any or little homology of sequences.
- The conclusion of the examiner is that the "Regenmortel's reference anticipated the current invention." I do not believe there is a single immunologist who works with peptide protein antigens and epitopes who would agree with the latter conclusion. As stated above, the invention of Calenoff-Ditlow is the peptide selection method and the compositions of the peptides selected by those methods both the methods and the peptides of Calenoff-Ditlow are neither described nor hinted at in the Regenmortel paper.
- d. Under claim rejections 35 USC number 103, part 3:
   The examiner rejects claims 18-19 because:

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"Regenmortel teaches using recombinant technology ----- to synthesize peptides capable of producing immunogenicity ---." Any peptide, including mimotope peptides, could potentially be used as immunogens, as the examiner states, by coupling to a carrier molecule to enhance immunogenicity. However, as pointed out above, it is incorrect to use the mimotope example in Regenmortel, or in any other way by anyone, in comparison or in relation to the identified peptide sequences from the target proteins as described by Calenoff-Ditlow. Thus, the premise used by the examiner is incorrect.

e. Under part 4: The examiner rejects claim 22 using the example of IL-2 to induce immune tolerance to specific respiratory antigens. IL-2 is a protein with defined biologic activities including the example cited by the examiner. The PSP sequences selected by the invention of Calenoff-Ditlow are peptides and a part of a protein, the target protein. One cannot equate the protein and peptides of the Tu et al. reference and the Calenoff-Ditlow patent application; the protein and peptides are quite different entities, both as they are defined, and as they are exist structurally - IL-2 has a defined 3D secondary and tertiary structure whereas Calenoff-Ditlow peptides, as free peptides or as conjugated to a carrier molecule, will more likely exhibit multiple secondary structures over any time interval (such peptides would be termed to have "random" structure).

Finally, I am unaware of any previous work or reports other than Calenoff-Ditlow of the invention disclosed in the patent application captioned above. I believe the patent application captioned above discloses an invention that is a contribution to the field of immunology.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the Untied States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

> Respectfully Submitted, Mr E Onlerson

Byron Anderson

7/16/04

#### CURRICULUM VITAE

#### Byron E. Anderson

Date of Birth:

December 30, 1941;

1941; Hammond,

Indiana

Education:

B.A.

1963

Kalamazoo College,

Kalamazoo,

Michigan;

Chemistry and Biology

Ph.D.

1968

University of Michigan, Ann Arbor, Michigan; Biochemistry; also student at John Hopkins University, Baltimore, Maryland

1966-1968.

Thesis Advisor: Dr. Saul Roseman

#### Positions Held:

**Postdoctoral Fellow** - 1968-1971, Columbia University, College of Physicians and Surgeons, New York, New York. Advisor: Dr.Elvin A. Kabat.

Assistant Professor, Departments of Biochemistry, and Otolaryngology and Maxillofacial Surgery, Northwestern University Medical School, 1971-1977.

**Associate Professor**, Departments of Biochemistry, and Otolaryngology and Maxillofacial Surgery, Northwestern University Medical School, 1977-1982.

**Associate Professor**, Department of Molecular Biology and Biochemistry Program 1982-1984.

· **Professor**, Departments of Molecular Biology, and Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, 1984-1989.

**Professor**, Departments of Cell and Molecular Biology, and Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, 1989-present.

Professor, Department of Urology, 1995 - present.

Member, Cancer Center, 1975 -

Member, Arthritis Research Program, 1976 - ; Multipurpose Arthritis Center, 1983 -

Member, Tumor Cell Biology Program, 1979 -

Member, Interdisciplinary Program in Molecular, Cellular and Integrative Biomedical Sciences, 1983 - 1990.

Member, Molecular and Cellular Biology Training Program, 1983 -

Member, Medical Scientist Training Program, 1985 -

Member, Biotechnology Training Program, 1993 -

#### Honors and Fellowships:

1974-1979, Research Career Development Awardee of NIH (NIAMDD)

1973-1974, Senior Investigator of the Arthritis Foundation

1968-1971, Postdoctoral Fellow of the Helen Hay Whitney Foundation and the National Cystic Fibrosis Research Foundation

1963-1968, United States Public Health Service Trainee

1963, summer National Science Foundation Undergraduate Trainee

#### Professional Societies and Activities:

American Association for the Advancement of Science American Society of Biochemistry and Molecular Biology American Association of Immunologists International Society for Oncodevelopmental Biology and Medicine

Society for Complex Carbohydrates American College of Rheumatology International Society for Artificial Organs The Protein Society

Advisor or Consultant to a number of biotechnology companies: Sangtec Medical, Fresenius, Abbott Labs., Chugai Pharm. LTD, Vivex Therapeutics, Inc., Carbohydrates Int., Toagosei Pharm.

#### Students:

iics.	
Celia Kaye, Ph.D.,	1976
Linda Hanson, M.S.,	1976
Margaret Steffes, M.S.,	1977
Lorraine Gill, Ph.D.,	1977
Tod Sloan, Ph.D.	1979
John Jay Weiss, M.S.,	1979
Lyman Davis, M.S.,	1980
Mark Pankow, M.S.,	1983
Lyman Davis, Ph.D.	1984
Ruth Entiwstle, Ph.D.,	1986
John Jay Weiss, Ph.D.,	1986
Mark Pankow, Ph.D.,	1988
Michael Baumann, Ph.D.,	1990
Michael Shields, Ph.D.,	1991
John J. Kresl, Ph.D.,	1992
Marilyn Brown, Ph.D.,	1992
Winnie Pao, M.S.	1993
NaMi Cho, M.S.,	1994
Joseph Orlando, M.S.,	1994
Sanjiv Gupta, M.S.,	1994
Katherine Worthington, Ph.D.,	1994
Jai Syn, M.S.,	1995
Cristopher Olenec, M.S.	1995
Lora Tucker-Garcia, M.S.	1995
Uri Ratner, M.S.	1996
Christina Stadler, M.S.	1996
Lora Kastrup, M.S.	1996
Marsha Yoder, M.S.	1997
Jasbir Kindra, M.S.	1997
Sharon Doering, M.S.	1997
Clara Smith, M.S.	1998
Ethan Buckley, M.S.	1999
Scott Rosenblum, M.S.	2000
Nancy Sullivan, M.S.	2000
Jeffery Black, M.S.	. 2000

#### Trainees:

#### Postdoctoral Fellows:

Deepika Paul	Mario Venegas
Samar Maklouf	Thomas Rohr
Jitendra Verma	Michio Tanaka
Shiva Motameni	Stewart Nelson
Lyman Davis	Ramendra Pandey
Bernard Kubak	Donna Bishop

#### Residents in Rheumatology:

Mike Repice

Albert Iammartino

Charlotte Harris

William Liu

Cynthia Gustafson

#### Residents in Otolaryngology:

Deyan Popovic

Susan Lyon

#### Medical Students:

James Carr

Robert Sobut Sarah Keesara

Denise Mistro Ragu Thunga

Susan Roth Thomas Walsh

Thomas Lucke Thomas Henthorn Paul Lyon

Martin Radvany

Ateet Shah

Tapubrata Ghosh Annette Barns

Reeva Shulruf

James Misak Samir Taneja Ripal Ghandi

Roberta Gausas William Walsh

Kyle ver Steeg

Sylvester Black

#### Biotechnology Program Students:

Winnie Pao

Cristina Stadler Christopher Olenec Marcia Yoder Jasbir Kindra

Ayano Takamoto Lourdes Bermejo

Jai Syn Nami Cho Joseph Orlando

Uri Ratner Sanjiv Gupta Ethan Buckley

Sharon Doering Scott Rosenblum Lora Kastrup Clara Smith Nancy Sullivan

Jeffrey Black

Undergraduate Students:

Marlene Morrison

Loretta Liu John Zachariah Jennifer Shaw Jason Roh

Daniel Fryxell Michael Baumann Ragu Thunga

Denise Mistro Askok Kukadia Andrew Hong Kirsten Stadler

Martin Radvany Andrew Radvany

Daniel Roh

Gautham Reddy Stephanie Wu

SandyShaw

David Napochi

Katherine Chen

Thomas Kim

#### Students, Thesis, Present Position

Celia Kaye, M.D., Ph.D.

Cystine Reduction and Transport in Cystinotic and Normal Fibroblasts

Ph.D., Biochemistry, 1985

Head, Genetics, U. of Texas, San Antonio

Linda Hanson, M.S.

Characteristics of the Antigenic Reactivities of Rheumatoid Arthritic Synovial Fibroblasts
M.S., Clinical Pathology, 1976

Lorraine Gill, Ph.D.

Characterization of Reactivities of Anti-Cellular Sera with Tumor Cells in Vitro

Ph.D., Biochemistry, 1977

Research Scientist, New England Nuclear

Margaret Lu Steffes, M.S.

Delineation and Partial Characterization of an Associated Rhematoid Arthritic Reactive Antigen

M.S. Biochemsitry, 1977

Senior Manager, Abbott Labs

Tod B. Sloan, M.D., Ph.D.

A Study of Synovial Cell Antigens

Ph.D., Biochemsitry, 1978

Associate Professor, Dept. Anesthesiology, U. of Texas, San Antonio

John Jay Weiss, M.S., Ph.D.

Studies on the Platelet Derived Connective Tissue Activating Peptide

M.S., Clinical Pathology, 1979

Program Director in Allergy, Diagnostic Products Corp.

Lyman E. Davis, M.S., Ph.D.

Immunoassays for Fibronectin

M.S., Clinical Pathology, 1980

Senior Director, Takeda Abbott

Mark L. Pankow, M.S., Ph.D.

Immunochemical Staining of Cancer Tissues

M.S., Clinical Pathology, 1983

Director of R&D, Parke DeWatt Labs

#### Students, Thesis, Present Position - continued

Lyman E. Davis, M.S., Ph.D.

Specificities of Antibodies to a Carbodiimide and to the Amino-Terminus of a Platelet Mitogen Ph.D., Tumor Cell Biology, 1984
Senior Director, Takeda Abbott

Ruth A. Entwistle, Ph.D.

A Kinetic Study of Fibronectin and the Clq Component of Complement  $\operatorname{Ph.D.}$ ,

Tumor Cell Biology, 1986

Research Associate, Washington U. School of Medicine

Mark L. Pankow, M.S., Ph.D.

Development of an Assay for Detection of Galactose Terminated Glycoprotiens in Biologic Fluids Ph.D., Tumor Cell Biology, 1988 Director of R&D, Parke DeWitt Labs.

John Jay Weiss, M.S., Ph.D.

Studies of Complement Mediated Interactions Between Fibronectin and Immune Complexes Ph.D., Tumor Cell Biology, 1989 Program Director in Allergy, Diagnostic Products Corp.

Michael A. Baumann, Ph.D.

Synthetic Peptides with Immune Complex Binding Activity Ph.D., Tumor Cell Biology, 1990 Research Scientist, Abbott Labs.

Michael J. Shields, Ph.D.

Characterization and Use of Monoclonal and Polyclonal Antibodies

Directed Against C-Reactive Protein in the Fluid and Solid Phase

Detection of Altered Forms of C-Reactive Protein in Humans Ph.D., Molecular Biology, 1991

Postdoctoral Fellow, National Institutes of Health

#### Students, Thesis, Present Position - continued

John Joseph Kresl, Ph.D., M.D.

Evaluation of Native Modified Human C-Reactive Protein

Interconversion: Possible Role for Modified C-Reactive

Proteins in Tumor Inhibition

Ph.D., Tumor Cell Biology, 1992, MD, 1993

Staff Physician, Radiation Oncology, St. Mary's

Hospital, Phoenix,

Marilyn R. Brown, Ph.D.

Receptor-Ligand Interactions Between Serum Amyloid P

Component

and Model Soluble Immune Complexes

Ph.D., Tumor Cell Biology, 1993

Research Scientist, Baxter Labs.

Winnie Pao, M.S.

Autoantibodies in Colon Cancer

M.S., Biotechnology Program, 1993

Research Associate, Division of Transplantation, NUMS

Katherine Worthington, Ph.D.

Design of Peptides Binding to Beta-2-microglobulin and

Immunoglobulin G

Ph.D., Tumor Cell Biology, 1994

Research Analyst, Research Corp. Technologies

NaMi Cho, M.S.

Binding of IgG Aggregates to CBP2-Amino Link

M.S., Biotechnology Program, 1994

Postdoctoral Fellow, Boston University

Joseph Orlando, M.S.

CBP2 Binding of Aggregated-IgG

M.S., Biotechnology Program, 1994

Graduate Student, Dept. of Microbiology-Immunology,

Wake Forest University, Bowman Gray School of Medicine

Sanjiv Gupta, M.S.

Detection of a Transferrin Isoform Associated with Alcohol

Consumption

M.S., Biotechnology Program, 1994

Medical Student, University of Indiana

#### Students, Thesis, Present Position - continued

Jai Syn, M.S.

Specificities of Binding of Lectins to an Aromatic Carbohydrate Mimetic Library M.S., Biotechnology Program, 1995 Research Associate, Abbott Labs.

Christopher Olenec, M.S.

Binding of Proteins to a Secondary Structure Limited Peptide Library

M.S. Biotechnology Program, 1995.

U.S. Commerce Dept. on FDA Regulations, Washington, D.C.

Lora Tucker-Garcia, M.S.

Carbohydrate Deficient Glycoproteins: Significance in Carbohydrate Deficient Glycoprotein Syndrome, Alcoholism, and Fetal Alcohol Syndrome M.S., Biotechnology Program, 1996 Research Associate, Abbott Labs.

Uri Ratner

Characterization of Xenoreactive Antibodies Important in Transplant Rejection M.S. Biotechnology program, 1996 Research Analyst, Venture One

Cristina Stadler

Complement Inhibition by Peptides in Hyperacute Rejection Reactions
M.S., Biotechnology Program, 1996

Division Manager, Baxter Labs.

Lora Kastrup Study of Vaginal Fluid Oligosaccharides in UTIs M.S., Biotechnology Program, 1996 Research Associate, Baxter Healthcare Corporation

Jasbir Kindra, M.S., LL.D.

Complement Inhibition Through the Use of Diaromatic Peptides to Allow Xenotransplantation

M.S., Biotechnology Program, 1997

Patent Attorney, Green Bay, WI

#### Students, Thesis, Present Position

Marcia Yoder, M.S. Studies on Complement Inhibition by a Diaromatic Peptide, Tryptophan-Tyrosine M.S., Biotechnology Program, 1997 Research Associate, Eli Lilly Co.

Sharon Doering, M.S. Avian IgY antibodies - Use in Xenotransplantation M.S., Biotechnology Program, 1997 Biotechnology Analyst, Madison Securities

Clara Smith, M.S.
Cross-Linked Avian IgY and Human IgG as Potential
Inhibitors of Rejection in Xenotransplantation
M.S., Biotechnology Program, 1998
Research Scientist, Glaxo Welcome

#### Committee Service:

Research Committee, Medical and Dental Schools

Sigma XI Symposia

Medical Applicant Interview

Cancer Center Library

General Services Committee of Faculty Senate

Faculty Senate

Biochemistry Workshop

Departmental Outside Speaker, Equipment, Library

Graduate Affairs Committee

VA Research Development Committee

Executive Committee of the Biochemistry Program

Cancer Center Equipment

Cancer Focus

Medical Admissions

Tumor Cell Biology Program

Comprehenisve Examination

Pre-Thesis and Thesis Committees for 33 students

University Research Grants Committee

General Faculty Committee

Graduate Professional Education of the Physician

Task Force on the Future of the Medical Library

Microbiology Department Review Committee

Medical Senate Council

Medical Council

Medical Library Long-Range Planning Committee

Program Review of Microbiology-Immunology

Program Review of Physical Therapy Curriculum

Research Program Committee on Immunobiology

Intellectual Property Committee

Medical School Urology Chair Search Committee

Medical School Division Making Course Development Committee

Medical School Research Council

Biotechnology Program:

Executive

Committee,

Admissions,

Advisory Board

Honors Program in Medical Education

Program Review Committee - Mol. Pharm. & Biochem.

# Committee Service 1984 - University:

General Faculty Committee, 1982-1985
Subcommittee on Benefits
Chair, GFC/Trustees Meeting, 1983, 1984
Intellectual Property Committee, 1989-1996
University Research Grants Committee, 1973 - 1976;
1995 -

Biotechnology Program: Executive Committee, Admissions, Advisory Board, 1992 -

#### Medical School:

Medical Senate Council, 1984-1988
General Profession Education of the Physician
Committee

Chair, Subcommittee on Faculty Involvement, 1985-1986 Research Long-Range Planning in Immunobiology, 1985-1986

Chair, Research Program Committee on Immunobiology, 1985- 1990
Medical School Admissions, 1972 Honors Program in Medical Education, 1996 -

#### Departmental:

Appointments, Promotion, Tenure Graduate Affairs Course/Exam/Certificate - Chair Promotions - Chair Library Recruitment - Chair

#### Teaching Service:

- 1. Medical, Biochemistry, laboratory section
  Subjects: Statistics, acid-base balance,
  nutrition, automated analyses, topics
  in immunology and autoimmune diseases
- 2. Medical, Biochemistry, lecture Topics: glycogen metabolism mucopolysaccharides, saccharide interconversions glycoproteins hexose monophosphate pathway post-ribosomal processing of proteins
- 3. Medical, biochemistry, lecture and independent study of immunology with students with proficiency in biochemistry
  - 4. Medical, immunology, lectures on antibody structure

    and antibody antigen interactions
  - 5. Medical, basic oncology, lectures on biological membranes
  - 6. Graduate, survey course in immunology
- 7. Graduate, lecture and seminar on biological membrane topics
- 8. Graduate, lectures in immunlology on antibody structure, antigenic determinants, antibody-antigen interactions, antibody functions
  - 9. Graduate, survey courses in biochemistry,
    Topics: carbohydrate sturcture, analysis;
    glycoprotein and glycolipid stucture,
    functions and metabolism;

lipopolysaccharide

structure and synthesis; biological membranes; muscle structure protein structure protein - ligand binding

enzyme mechanisms enzyme kinetics

- 10. Graduate, basic oncology, lectures on biologic membranes
- 11. Graduate, survey course in immunochemistry
- 12. Post-Graduate, lecture on inter-relationships of comple-ment, fibrinolytic and kinin systems

#### LECTURES, MEDICAL BIOCHEMISTRY

- 1. Glycogen metabolism and regulation
- Structural complementarily, amplification of metabolic response, disorders in glycogen metabolism
- 3. Galactose, glucuronic acid metabolism, mucopolysaccha-rides, saccharide interconversions, hexose monophosphate shunt
- 4. Post-ribosomal modification of proteins, protein polymorphisims and disease consequences
- 5. Fatty acid synthesis and degradation
- 6. Lipid structure and function
- 7. Phospholipid structure and function

#### BASIC ONCOLOGY:

- 1. Structural features of biologic membranes
- 2. Tumor cell membranes, tumor-associated antigens

#### GRADUATE BIOCHEMISTRY:

- 1. Stereochemistry of carbohydrates
- 2. Conformations of carbohydrates
- 3. Chemical reactivity and conformation
- Methodology for structural determinations of carbohydrate sequences
- 5. Types and characteristics of complex carbohydrates
- 6. Methods applied to analysis of complex carbohydrates
  - 7. Synthesis of complex carbohydrates
  - 8. Functions of complex carbohydrates
  - 9. Proteins primary and secondary structure
  - 10. Proteins Tertiary and quaternary structure
  - 11. Protein-protein and protein-ligand interactions
  - 12. Proteins structural predictions
  - 13. Enzyme kinetics
  - 14. Enzyme mechanisms
  - 15. Enzymes Types and regulation

- 16. Membrane structure and function
- 17. DNA and RNA structures
- 18. Principles that determine polynucleotide structure
- 19. Protein polynucleotide interactions

#### LECTURES, DENTAL BIOCHEMISTRY

- 1. Glycogen metabolism and regulation of blood glucose
- 2. Structure and function of phospholipids, membrane structure
- 3. Fatty acid synthesis and degradation
- 4. Interrelationships and regulation of metabolic pathways

#### IMMUNOCHEMISTRY:

- Heterogeneity of the antibody response; classes, subclasses, allo- and idiotypes of Igs
- Structural features of Igs; discussion of homologies and deduction of structure from amino acid sequence data
- 3. Effector functions of the Iqs
- 4. Three dimensional structure of Igs and quaternary interactions of domains
- 5. Antibody combining site constructs
- 6. Antibody combining site interactions with haptens; serologic specificities
- Measurement, interpretation and quantitations of antibody-antigen interactions
- 8. Kinetic analyses of antibody-hapten interactions
- 9. Radio- and enzyme-immunoassays
- 10. Parameters of antigenicity and immunogenicity

#### CANCER PHARMACOLOGY:

- 1. Progression and selection of tumor cell populations; changes in cell surface composition and interactions with metastases
- 2. Tumor-associated antigens

#### RESIDENT AND STAFF LECTURES:

Otolaryngology: lectures on overview of tumor immunology

Rheumatology:

- Synovial cell metabolism and antigen, genetic analysis of antigen expression
- Protein Polymorphisms:
   types, effects on protein
   function, contribution to
   disease processes

#### Subjects taught in Medical Biochemistry Laboratory:

- 1. Principles and methods of automated analyses
- 2. Acid-base regulation and imbalances
- 3. Statistical methods and analyses of clinical data
- 4. Dietary calculations of protein, carbohydrate, lipid, caloric intake and nitrogen balance
  - 5. Presentations, analysis, critique of primary clinical and basic research papers

#### Current Teaching:

Lectures in graduate biochemistry: Characterizations

of proteins, protein secondary, tertiary and quaternary structures, predictions of protein and peptide structures, binding site interactions of proteins with various ligands, structures of polynucleotides, chemistry, stereochemistry and conformations of carbohydrates, structural types of complex carbohydrates, complex carbohydrates biosynthesis, functions of complex carbohydrates.

Lectures in medical and dental biochemistry: on carbohydrate, lipid and phospholipid structure and function, glycogen metabolism and regulation of blood glucose, fatty acid synthesis and degradation, and integration and regulation of carbohydrate and lipid metabolism.

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# <u>Carbohydrate Sequence Epitopes and Anti-Carbohydrate</u> Specificities

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Abstract: Fryer, J., Ivancic, D., Zhang, J., Leventhal, J., Blondin, B., Kaufman, D., Abecassis, M., Stuart, F. and Anderson, B., "Induced Anti-Porcine Endothelial Cell (PEC) Xenoantibodies (XAbs) Upregulate E-Selectin and VCAM Expression," 5<sup>th</sup> Cong. Int. Xenotransplantation Assoc., Kyoto, Oct., 1999.

Fryer, J. P., Zhang, Z., Roslkowski, J., Pao, W., Niekrasz, M., Leventhal, J., Abecassis, M. and Anderson, B., "Isotype and IgG Subtype Switches Associated with an Elicited Primate Xenoantibody Response to Non-alphaGal Porcine Endothelial Antigens," Am. Soc. Transplantation, Chicago, May, 2000.

# Transplantation Studies - continued

Tishler, D. S., Fryer, J. P., Anderson, B., Ivancic, D., Leventhal, J. and Zhang, Z., "Temporal Characterization of Anti-alphaGal Mediated cardiac Graft Rejection in a Murine Model," Am. Soc. Transplantation, Chicago, May, 2000.

Leventhal, J., Su, A., Kaufman, D., Abecassis, M., Anderson, B. and Fryer, J. P., "Altered Infectivity of Porcine Endogenous Retrovirus by Protective Avian Antibodies: Implications for Pig - Human Xenotransplantation," Am. Soc. Transplantation, Chicago, May, 2000.

Kim, T. and Anderson, B., "Isolation and Characterization of Human Anti-alphaGal Antibodies," Am. Soc. Adv. Sci., Am. Jun. Acad. Sci., Washington, D.C., Feb., 2000.

Fryer, J. P., Firca, J., Leventhal, J. R., Blondin, B., Malcolm, A., Ivancic, D., Gandhi, R., Shah, A., Pao, W., Abecassis, M., Kaufman, D. B., Stuart, F. and Anderson, B. E., Igy Anti-Porcine Endothelail Cell Antibodies Effectively Block Human Anti-Porcine Xenoantibody Binding," Xenotransplantation, 56, 98 - 109, 1999.

Fryer, J. P., Leventhal, J. R., Pao, W., Stadler, C., Jones, M., Walsh, T., Zhong, R., Zhang, Z., Wang, H., Goodman, D. J., Kurek, M., d'Apice, A. J. F., Blondin, B., Ivancic, D., Buckingham, F., Kaufman, D., Abecassis, M., Stuart, F. and Anderson, B. E., "Sysnthetic Peptides which Inhibit the Interaction between Clq and Immunoglobulin and Prolong Graft Survival," Transplantation, 70 828 -836, 2000.

Walsh, W.E., Anderson, B. E., Ivancic, D., Zhang, Z., Paccini, J. P., Rodgers, T. G., Pao, W. and Fryer, J. P., "Distribution of and Immune Response to Chicken antialphaGal Immunoglobulin Y Antibodies in Wild-Type and alphaGal Knockout Mice," Immunology, 101, 1 - 11, 2000.

Cook, C. L., Pao, W., Firca, J. R., Anderson, B. E. and Fryer, J. P., "Simple Purification Methods for alphaGalactose-Specific Antibody form Chicken Eggs,", J. Biosci. & Bioeng., 91, 305 - 310, 2001.

### Other Studies

Carruthers, M. and Anderson, B., "Inhibition by Polyanions of Vibrio Parahaemolyticus Adherence: A Physiochemical Effect", J. Inf. Dis., 140, 119-122, 1979.

Jemmerson, R., Kaplan, B., Denton, M.D., Anderas, P., Anderson, B. and Margoliash, E., "Six Related Protein Products from a Single Patient with Multiple Myeloma," Biochemistry, 18, 4676-4683, 1979.

Anderson, B., Donakowski, C., Entwistle, R. and Davis, L., "Reisolation of Immunoreactive Radioiodinated Antigens Using Glutaraldehyde-Insolubilized Antibody Preparations," J. Immunological Methods, 36, 309-314, 1980.

Davis, L.E., Roth, S.A. and Anderson, B., "Antisera Specificities to 1-Ethyl-3-(3-Dimethylaminopropyl) Carbodiimide Adducts of Proteins," Immunology, 53, 435-441, 1984.

Abstract: Cohen, I., Drisdel, R.C. and Anderson, B., "Factor XIII-Catalyzed Polymeric Assemblies in Platelets," 32nd Meeting of the International Committee on Thrombosis and Hematology, Jerusalem, June, 1986.

Pandey, R., Davis, L.E., Anderson, B. and Hollenberg, P.F., "Photoaffinity Labeling of Primary Aromatic Amines to Carrier Proteins to Elicit Antibody Response Against the Amine Haptens," J. Immunol. Methods, 94, 237-246, 1986.

Cohen, J. and Anderson, B. "Immunochemical Characterization of Transglutaminase-Catalyzed Polymers of Activated Platelets," <u>Thromb. Res.</u>, <u>47</u>, 409-416, 1987.

Abstract: Koch, A.E., Burrows, J.C., Marder, R., Domer, P., Anderson, B. and Leibovich, S.J., "Preliminary Characterization of Monocyte/Macrophage (mo) Heterogeneity using Monoclonal Antibodies Generated to U937 Cells and Human Rheumatoid (RA) Tissue Synovial Macrophages," 4th International Conference on Leukocyte Differentiation Antigens, Tissue Antigens, 33, 205 1988.

### Other Studies - continued

Abstract: Koch, A.E., Burrows, J.C., Marder, R., Domer, P., Anderson, B. and Leibovich, S.J., "Monocyte/Macrophage (mo/mo) Heterogeneity Defined by a Panel of Monoclonal Antibodies Produced to Rheumatoid (RA) Synovial Tissue Mo," American Federation for Clinical Research, Clin. Res., 37, 413A, 1989.

Abstract: Kim, J.G., Miller, M.M., Anderson, B., Rebar, R.W. and LaBarbera, A.R., "Anti-Ovarian Antibody Titers Correlate with Serum FSH Concentrations in Experimentally Induced Ovarian Failure," Soc. Gynecologic Investigation, March, 1989.

Clark, C.R., Kresl, J.J., Hines, K.K. and Anderson, B.E., "An Immunofiltration Apparatus for Accelerating the Visualization of Antigen on Membrane Supports," Anal. Biochem., 228, 232-237, 1995.

Abstract: Kim, J.G., Anderson, B.E., Rebar, R.W. and LaBarbera, A.R., "Determination by ELISA of Anti-ovarian Antibodies in Premature Ovarian Failure," Am. Fertility Soc., Nov., 1989.

Abstract: Pankow, M.L., Cane, R. and Anderson, B., "Development of Enzyme-Linked Lectin Assay for the Detection and Quantitation of Desialylated Serum Glycoproteins," Fed. Proc., 45, 3359, 1986.

Abstract: Pankow, M.L., Cane, R. and Anderson, B., "Quantitation in Sera of Desialylated Glycoproteins using an Antibody and Lectin Sandwich Assay," Soc. Complex Carbohydrates, Charleston, S. C., Nov. 1986.

Abstract: Clark, C., Kresl, J., Hines, K., Anderson, B. and Mallia, A.K., "An Apparatus for Rapid Detection of Western and Dot-Blotted Proteins," FASEB J., 5, A913, 1991.

Abstract: Davis, L., Jokinen, D., Turk, L., Radvany, M., Theophilus, A., Fitzsimons, E. and Anderson, B., "Immunoassays for Hemoglobin Alc Employing Antibodies Directed to a Reductively Modified Peptide Immunogen." FASEB J., 5, A913, 1991.

# Other Studies - continued

Koch, A.E., Burrows, J.C., Marder, R., Domer, P., Anderson, B. and Leibovich, S.J., "Monoclonal Antibodies Detecting Monocyte/Macrophage Activation and Differentiation Antigens and Identifying Functionally Distinct Subpopulations of Human Rheumatoid Synovial Tissue Macrophages," Am. J. Path., 138, 165-173, 1991.

Kim, J.G., Anderson, B.E., Reban, R.W. and LaBarbera, A.R., "A Biotin-Streptavidin Enzyme Immunoassay for Detection of Antibodies to Porcine Granulosa Cell Antigens," J. Immunoassay, 12, 447-464, 1991.

Abstract: Holloran, M.M., Haskell, C.J., Carley, W., Shah, M.R., Anderson, B. and Koch, A.E., "4All: A Cytokine-Inducible Endothelial Antigen," J. Invest. Med., 43, 335A, 1995.

Clark, C.R., Kresl, J.J., Hines, K.K. and Anderson, B.E., "An Immunofiltration Apparatus for Accelerating the Visualization of Antigen on Membrane Supports", Anal. Biochem., 228, 232-237, 1995.

Woods, J. M., Campbell, P. L., Polverini, P. J., Anderson, B. and Koch, A. E., "The Soluble 4All Antigen is Angiogenic in vivo and is Upregulated in Rheumatoid Arthritis Compared to Osteoarthritis Synovial Fluid and Serum, submitted for review.

Abstract: Woods, J. M., Campbell, P. L., Polverini, P. J., Anderson, B. E. and Koch, A. E., "The Soluble 4All Antigen is Angiogenic in vivo and is Upregulated in Rheumatoid Arthritis Compared to Osteoarthritis Synovial Fluid and Serum," Assoc. Clin. Res. Mtg, Nov., 1997, Washington, D.C.

Abstract: Woods, J. M., Campbell, P. L., Polverini, P. J., Anderson, B. E. and Koch, A. E., "The Soluble 4All Antigen is Angiogenic in vivo and is Upregulated in Rheumatoid Arthritis Compared to Osteoarthritis Synovial Fluid and Serum," Am. Fed. Med. Res., April, 1998, J. Inv. Med., 46, 233A, 1998.

### PATENT APPLICATIONS

1. Binding of immune complexes by modified forms of creactive protein.

Applicants: Northwestern University and

Rush - Presbyterian - St. Luke's Medical Center

Inventors: Potempa and Anderson

U.S. application Serial No. 07/582,884,

Filed: October 3, 1990

Refiled: 08/271,137; July 6, 1994 - 2545/73

Status: Issued: January 14, 1997; US Letter

Patent No. 5,593,897

PCT application number PCT/US89/01247

Filed March 31, 1989 (2545/11)

Status: Nationalized

Australian application no. 34485/89 Filed: March 31, 1989 (2545/24)

Status: Issued, 6/11/93; Serial #633488

Japanese application No. 1-504716 Filed: March 31, 1989 (2545/26)

Status: Pending, awaiting examination

Canadian application No. 595,543 Filed April 3, 1989 (2545/10) Status: Pending, no action yet

EPO application No. 89904944.9 Filed March 31, 1989 (2545/25)

2. A synthetic peptide and its uses Applicant: Northwestern University

Inventors: Baumann and Anderson

U.S. application Serial No. 07/598,416

Filed: October 16, 1990 (2545/28)

Status: Issued November 15, 1994

Patent Number 5,364,930

PCT application number PCT/US91/07581

Filed: October 9, 1991

Status: Pending

### PATENT APPLICATIONS- continued

3. Binding of aggregated immunoglobulin or immune complexes by serum amyloid P component Applicant: Northwestern University Inventors: Anderson and Brown U.S. application Serial No. 07/672,526

Filed: March 19, 1991 (2545/21) Status: Issued 6/22/93, P-5,221,628

4. Immunoassay for glycosylated proteins employing antibody to reductively glycosylated amino acids Applicant: Northwestern University

Tryontone: Northwestern onivers

Inventors: Davis and Anderson

U.S. application Serial No. 07/397,781 (2545/5)

08/068,525 (5/27/93) (2545/51) 08/151,073 (11/12/93) (2545/52)

Filed: August 23, 1989

Status: Granted; U.S. Letters Patent No. 5,484,735

PCT application no. PCT/US90/04666 Filed: August 17, 1990 (2545/23)

Status: Nationalized

EPO application no. 90913261.5

Filed: August 17, 1990 (2545/37)

Status: Granted

Japanese application no. 2-512516

Filed: August 17, 1990 (2545/38)

Status: Pending, awaiting examination

#### PATENT APPLICATIONS - continued

5. Immunoassay for detecting and monitoring alcoholics
Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Makhlouf, Pankow, Anderson and Bean

U.S. application Serial No. 07/765,169;

Filed: September 25, 1991 (2545/8)

08/272,852; July 08, 1994 (2545/74)

Status: granted

PCT application Serial No. PCT/US92/08136 Filed: September 25, 1992 (2545/44)

Status: Nationalized

EPO application no. 92921176.1

Filed: August 25, 1992 (2545/60), granted

Japanese application no. 5-506376

Filed: 9/25/92 (2545/61)

Canadian application no. 2119651 Filed: 9/25/92 (2545/59), granted

Australian application no. 27577/92 Filed 9/23/92 (2545/58), granted

6. Methods of Treating Cancer Using Modified C-Reactive Protein

Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Potempa, Kresl and Anderson

U.S. application Serial No. 07/874,263

Filed: April 24, 1992

Status: Issued December 12, 1995

US Letters Patent No. 5,474,904

PCT application no. PCT/US/03769

Filed: 4/22/9

4/22/92 (2545/50)

Status: Nationalized

EPO application no. 93910710.8, Filed: 4/22/93

(2545/81)

Japanese application no.5-518361, Filed: 4/22/93 (2545/80)

Canadian application no. 2432001, Filed: 4/22/93 (2545/80)

Australian application no. 41109/93, Filed: 4/22/93 (2545/79)

### PATENT APPLICATIONS- continued

Method of detecting cancer

Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Anderson and Davis

U.S. application Serial No. 07/939,830

Filed: September 3, 1992 (2545/9) Status: Issued December 27, 1994

Patent Number 5,376,531

Japanese application No. 4-293052 Filed: October 30, 1992 (2545/45)

Status: Pending

8. Methods of Imaging Cancer Cells Using Modified C-

Reactive Protein

Applicant: Northwestern University

Inventors: Potempa, Kresl and Anderson

U.S. Application 149,663

Filed Nov. 9, 1993

Status: Issued December 12, 1995

US Letters Patent No. 5,474,904

9. CIP to Synthetic Clq Peptide Fragments - use

transplantation

Applicant: Northwestern University Inventors: Baumann, Anderson and Fryer Filed: April 6, 1996 to US patent office

Status: granted

PCT of same:

Application and Inventors: Baumann, Anderson and Fryer

April 4, 1997 Status: withdrawn

10. Method of Inhibiting Complement

Applicants and Inventors: Anderson and Fryer Filed: April 14, 1997 to US patent office

Status: granted

11. Peptides Comprising Aromatic D-Amino Acids and Methods

Of Use

Inventor: Byron E. Anderson US patent filed July 3, 2002

PCT application filed July 3, 2003

#### CURRICULUM VITAE

# Byron E. Anderson

Date of Birth: December 30, 1941; Hammond,

Indiana

Education:

B.A. 1963 Kalamazoo College, Kalamazoo,

Michigan;

Chemistry and Biology

Ph.D. 1968 University of Michigan, Ann Arbor,

Michigan; Biochemistry; also student at John Hopkins University, Baltimore, Maryland

1966-1968.

Thesis Advisor: Dr. Saul Roseman

#### Positions Held:

Postdoctoral Fellow - 1968-1971, Columbia University, College of Physicians and Surgeons, New York, New York. Advisor: Dr. Elvin A. Kabat.

Assistant Professor, Departments of Biochemistry, and Otolaryngology and Maxillofacial Surgery, Northwestern University Medical School, 1971-1977.

Associate Professor, Departments of Biochemistry, and Otolaryngology and Maxillofacial Surgery, Northwestern University Medical School, 1977-1982.

**Associate Professor**, Department of Molecular Biology and Biochemistry Program 1982-1984.

**Professor**, Departments of Molecular Biology, and Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, 1984-1989.

**Professor**, Departments of Cell and Molecular Biology, and Otolaryngology and Head and Neck Surgery, Northwestern University Medical School, 1989-present.

Professor, Department of Urology, 1995 - present.

Member, Cancer Center, 1975 -

Member, Arthritis Research Program, 1976 - ; Multipurpose Arthritis Center, 1983 -

Member, Tumor Cell Biology Program, 1979 -

Member, Interdisciplinary Program in Molecular, Cellular and Integrative Biomedical Sciences, 1983 - 1990.

Member, Molecular and Cellular Biology Training Program, 1983 -

Member, Medical Scientist Training Program, 1985 -

Member, Biotechnology Training Program, 1993 -

### Honors and Fellowships:

1974-1979, Research Career Development Awardee of NIH (NIAMDD)

1973-1974, Senior Investigator of the Arthritis Foundation

1968-1971, Postdoctoral Fellow of the Helen Hay Whitney Foundation and the National Cystic Fibrosis Research Foundation

1963-1968, United States Public Health Service Trainee

1963, summer National Science Foundation Undergraduate Trainee

### Professional Societies and Activities:

American Association for the Advancement of Science
American Society of Biochemistry and Molecular Biology
American Association of Immunologists
International Society for Oncodevelopmental Biology and
Medicine
Society for Complex Carbohydrates
American College of Rheumatology
International Society for Artificial Organs

International Society for Artificial Organs
The Protein Society

Advisor or Consultant to a number of biotechnology companies: Sangtec Medical, Fresenius, Abbott Labs., Chugai Pharm. LTD, Vivex Therapeutics, Inc., Carbohydrates Int., Toagosei Pharm.

# Students:

nts:	
Celia Kaye, Ph.D.,	1976
Linda Hanson, M.S.,	1976
Margaret Steffes, M.S.,	1977
Lorraine Gill, Ph.D.,	1977
Tod Sloan, Ph.D.	1979
John Jay Weiss, M.S.,	1979
Lyman Davis, M.S.,	1980
Mark Pankow, M.S.,	1983
Lyman Davis, Ph.D.	1984
Ruth Entiwstle, Ph.D.,	1986
John Jay Weiss, Ph.D.,	1986
Mark Pankow, Ph.D.,	1988
Michael Baumann, Ph.D.,	1990
Michael Shields, Ph.D.,	1991
John J. Kresl, Ph.D.,	1992
Marilyn Brown, Ph.D.,	1992
Winnie Pao, M.S.	1993
NaMi Cho, M.S.,	1994
Joseph Orlando, M.S.,	1994
Sanjiv Gupta, M.S.,	1994
Katherine Worthington, Ph.D.,	1994
Jai Syn, M.S.,	1995
Cristopher Olenec, M.S.	1995
Lora Tucker-Garcia, M.S.	1995
Uri Ratner, M.S.	1996
Christina Stadler, M.S.	1996
Lora Kastrup, M.S.	1996
Marsha Yoder, M.S.	1997
Jasbir Kindra, M.S.	1997
Sharon Doering, M.S.	1997
Clara Smith, M.S.	1998
Ethan Buckley, M.S.	1999
Scott Rosenblum, M.S.	2000
Nancy Sullivan, M.S.	2000
Jeffery Black, M.S.	2000

# Trainees:

# Postdoctoral Fellows:

Deepika Paul	Mario Venegas
Samar Maklouf	Thomas Rohr
Jitendra Verma	Michio Tanaka
Shiva Motameni	Stewart Nelson
Lyman Davis	Ramendra Pandey
Bernard Kubak	Donna Bishop

### Residents in Rheumatology:

Mike Repice

Albert Iammartino

Charlotte Harris

William Liu

Cynthia Gustafson

# Residents in Otolaryngology:

Deyan Popovic

Susan Lyon

#### Medical Students:

James Carr Thomas Lucke

Robert Sobut Sarah Keesara

Denise Mistro Ragu Thunga

Susan Roth Thomas Walsh

Thomas Henthorn Paul Lyon

Martin Radvany

Ateet Shah

Tapubrata Ghosh Annette Barns James Misak

Ripal Ghandi

Roberta Gausas

Reeva Shulruf Samir Taneja

William Walsh Kyle ver Steeg

Sylvester Black

# Biotechnology Program Students:

Winnie Pao Avano Takamoto

Cristina Stadler Christopher Olenec Marcia Yoder

Lourdes Bermejo

Jai Syn

Jasbir Kindra

Uri Ratner

Nami Cho

Joseph Orlando

Sanjiv Gupta

Sharon Doering

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Ethan Buckley Jeffrey Black

Scott Rosenblum

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# Undergraduate Students:

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Martin Radvany Andrew Radvany

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David Napochi

Jennifer Shaw Jason Roh Andrew Hong Kirsten Stadler

SandyShaw

Katherine Chen

Thomas Kim

### Students, Thesis, Present Position

Celia Kaye, M.D., Ph.D.

Cystine Reduction and Transport in Cystinotic and Normal Fibroblasts

Ph.D., Biochemistry, 1985

Head, Genetics, U. of Texas, San Antonio

Linda Hanson, M.S.

Characteristics of the Antigenic Reactivities of Rheumatoid Arthritic Synovial Fibroblasts
M.S., Clinical Pathology, 1976

Lorraine Gill, Ph.D.

Characterization of Reactivities of Anti-Cellular Sera with Tumor Cells in Vitro

Ph.D., Biochemistry, 1977

Research Scientist, New England Nuclear

Margaret Lu Steffes, M.S.

Delineation and Partial Characterization of an Associated Rhematoid Arthritic Reactive Antigen

M.S. Biochemsitry, 1977

Senior Manager, Abbott Labs

Tod B. Sloan, M.D., Ph.D.

A Study of Synovial Cell Antigens

Ph.D., Biochemsitry, 1978

Associate Professor, Dept. Anesthesiology, U. of Texas, San Antonio

John Jay Weiss, M.S., Ph.D.

Studies on the Platelet Derived Connective Tissue Activating Peptide

M.S., Clinical Pathology, 1979

Program Director in Allergy, Diagnostic Products Corp.

Lyman E. Davis, M.S., Ph.D.

Immunoassays for Fibronectin

M.S., Clinical Pathology, 1980

Senior Director, Takeda Abbott

Mark L. Pankow, M.S., Ph.D.

Immunochemical Staining of Cancer Tissues

M.S., Clinical Pathology, 1983

Director of R&D, Parke DeWatt Labs

# Students, Thesis, Present Position - continued

Lyman E. Davis, M.S., Ph.D.

Specificities of Antibodies to a Carbodiimide and to the Amino-Terminus of a Platelet Mitogen Ph.D., Tumor Cell Biology, 1984
Senior Director, Takeda Abbott

Ruth A. Entwistle, Ph.D.

A Kinetic Study of Fibronectin and the Clq Component of Complement Ph.D., Tumor Cell Biology, 1986

Research Associate, Washington U. School of Medicine

Mark L. Pankow, M.S., Ph.D.

Development of an Assay for Detection of Galactose Terminated Glycoprotiens in Biologic Fluids Ph.D., Tumor Cell Biology, 1988 Director of R&D, Parke DeWitt Labs.

John Jay Weiss, M.S., Ph.D.
Studies of Complement Mediated Interactions Between Fibronectin and Immune Complexes
Ph.D., Tumor Cell Biology, 1989
Program Director in Allergy, Diagnostic Products Corp.

Michael A. Baumann, Ph.D. Synthetic Peptides with Immune Complex Binding Activity Ph.D., Tumor Cell Biology, 1990 Research Scientist, Abbott Labs.

Michael J. Shields, Ph.D.

Characterization and Use of Monoclonal and Polyclonal Antibodies

Directed Against C-Reactive Protein in the Fluid and Solid Phase

Detection of Altered Forms of C-Reactive Protein in Humans Ph.D., Molecular Biology, 1991

Postdoctoral Fellow, National Institutes of Health

## Students, Thesis, Present Position - continued

John Joseph Kresl, Ph.D., M.D.

Evaluation of Native Modified Human C-Reactive Protein

Interconversion: Possible Role for Modified C-Reactive

Proteins in Tumor Inhibition

Ph.D., Tumor Cell Biology, 1992, MD, 1993

Staff Physician, Radiation Oncology, St. Mary's Hospital, Phoenix,

Marilyn R. Brown, Ph.D.

Receptor-Ligand Interactions Between Serum Amyloid P

Component

and Model Soluble Immune Complexes

Ph.D., Tumor Cell Biology, 1993

Research Scientist, Baxter Labs.

Winnie Pao, M.S.

Autoantibodies in Colon Cancer

M.S., Biotechnology Program, 1993

Research Associate, Division of Transplantation, NUMS

Katherine Worthington, Ph.D.

Design of Peptides Binding to Beta-2-microglobulin and

Immunoglobulin G

Ph.D., Tumor Cell Biology, 1994

Research Analyst, Research Corp. Technologies

NaMi Cho, M.S.

Binding of IgG Aggregates to CBP2-Amino Link

M.S., Biotechnology Program, 1994

Postdoctoral Fellow, Boston University

Joseph Orlando, M.S.

CBP2 Binding of Aggregated-IgG

M.S., Biotechnology Program, 1994

Graduate Student, Dept. of Microbiology-Immunology,

Wake Forest University, Bowman Gray School of Medicine

Sanjiv Gupta, M.S.

Detection of a Transferrin Isoform Associated with Alcohol

Consumption

M.S., Biotechnology Program, 1994

Medical Student, University of Indiana

## Students, Thesis, Present Position - continued

Jai Syn, M.S.

Specificities of Binding of Lectins to an Aromatic Carbohydrate Mimetic Library M.S., Biotechnology Program, 1995 Research Associate, Abbott Labs.

Christopher Olenec, M.S.

Binding of Proteins to a Secondary Structure Limited Peptide Library

M.S. Biotechnology Program, 1995.

U.S. Commerce Dept. on FDA Regulations, Washington, D.C.

Lora Tucker-Garcia, M.S.

Carbohydrate Deficient Glycoproteins: Significance in Carbohydrate Deficient Glycoprotein Syndrome, Alcoholism, and Fetal Alcohol Syndrome
M.S., Biotechnology Program, 1996
Research Associate, Abbott Labs.

Uri Ratner

Characterization of Xenoreactive Antibodies Important in Transplant Rejection
M.S. Biotechnology program, 1996
Research Analyst, Venture One

Cristina Stadler

Complement Inhibition by Peptides in Hyperacute Rejection Reactions M.S., Biotechnology Program, 1996 Division Manager, Baxter Labs.

Lora Kastrup Study of Vaginal Fluid Oligosaccharides in UTIs M.S., Biotechnology Program, 1996 Research Associate, Baxter Healthcare Corporation

Jasbir Kindra, M.S., LL.D.

Complement Inhibition Through the Use of Diaromatic Peptides to Allow Xenotransplantation

M.S., Biotechnology Program, 1997

Patent Attorney, Green Bay, WI

#### Students, Thesis, Present Position

Marcia Yoder, M.S.
Studies on Complement Inhibition by a Diaromatic Peptide,
Tryptophan-Tyrosine
M.S., Biotechnology Program, 1997
Research Associate, Eli Lilly Co.

Sharon Doering, M.S. Avian IgY antibodies - Use in Xenotransplantation M.S., Biotechnology Program, 1997 Biotechnology Analyst, Madison Securities

Clara Smith, M.S.
Cross-Linked Avian IgY and Human IgG as Potential
Inhibitors of Rejection in Xenotransplantation
M.S., Biotechnology Program, 1998
Research Scientist, Glaxo Welcome

#### Committee Service:

Research Committee, Medical and Dental Schools

Sigma XI Symposia

Medical Applicant Interview

Cancer Center Library

General Services Committee of Faculty Senate

Faculty Senate

Biochemistry Workshop

Departmental Outside Speaker, Equipment, Library

Graduate Affairs Committee

VA Research Development Committee

Executive Committee of the Biochemistry Program

Cancer Center Equipment

. Cancer Focus

Medical Admissions

Tumor Cell Biology Program

Comprehenisve Examination

Pre-Thesis and Thesis Committees for 33 students

University Research Grants Committee

General Faculty Committee

Graduate Professional Education of the Physician

Task Force on the Future of the Medical Library

Microbiology Department Review Committee

Medical Senate Council

Medical Council

Medical Library Long-Range Planning Committee

Program Review of Microbiology-Immunology

Program Review of Physical Therapy Curriculum

Research Program Committee on Immunobiology

Intellectual Property Committee

Medical School Urology Chair Search Committee

Medical School Division Making Course Development Committee

Medical School Research Council

Biotechnology Program:

ogram: Executive

Committee,

Admissions,

Advisory Board

Honors Program in Medical Education

Program Review Committee - Mol. Pharm. & Biochem.

# Committee Service 1984 - University:

General Faculty Committee, 1982-1985
Subcommittee on Benefits
Chair, GFC/Trustees Meeting, 1983, 1984
Intellectual Property Committee, 1989-1996
University Research Grants Committee, 1973 - 1976;
1995 -

Biotechnology Program: Executive Committee, Admissions, Advisory Board, 1992 -

#### Medical School:

Medical Senate Council, 1984-1988

General Profession Education of the Physician Committee

Chair, Subcommittee on Faculty Involvement, 1985-1986 Research Long-Range Planning in Immunobiology, 1985-1986

Chair, Research Program Committee on Immunobiology, 1985- 1990

Medical School Admissions, 1972 Honors Program in Medical Education, 1996 -

#### Departmental:

Appointments, Promotion, Tenure Graduate Affairs Course/Exam/Certificate - Chair Promotions - Chair Library Recruitment - Chair

## Teaching Service:

- 1. Medical, Biochemistry, laboratory section
  Subjects: Statistics, acid-base balance,
  nutrition, automated analyses, topics
  in immunology and autoimmune diseases
- Medical, Biochemistry, lecture Topics: glycogen metabolism mucopolysaccharides, saccharide interconversions glycoproteins hexose monophosphate pathway post-ribosomal processing of proteins
- 3. Medical, biochemistry, lecture and independent study of immunology with students with proficiency in biochemistry
  - 4. Medical, immunology, lectures on antibody structure and antibody - antigen interactions
  - 5. Medical, basic oncology, lectures on biological membranes
  - 6. Graduate, survey course in immunology
- 8. Graduate, lectures in immunlology on antibody structure, antigenic determinants, antibody-antigen interactions, antibody functions
  - 9. Graduate, survey courses in biochemistry,
    Topics: carbohydrate sturcture, analysis;
    glycoprotein and glycolipid stucture,
    functions and metabolism;

lipopolysaccharide

structure and synthesis; biological membranes; muscle structure protein structure protein - ligand binding

enzyme mechanisms enzyme kinetics

- 10. Graduate, basic oncology, lectures on biologic membranes
- 11. Graduate, survey course in immunochemistry
- 12. Post-Graduate, lecture on inter-relationships of comple-ment, fibrinolytic and kinin systems

#### LECTURES, MEDICAL BIOCHEMISTRY

- 1. Glycogen metabolism and regulation
- Structural complementarily, amplification of metabolic response, disorders in glycogen metabolism
- 3. Galactose, glucuronic acid metabolism, mucopolysaccha-rides, saccharide interconversions, hexose monophosphate shunt
- 4. Post-ribosomal modification of proteins, protein polymorphisims and disease consequences
- 5. Fatty acid synthesis and degradation
- 6. Lipid structure and function
- 7. Phospholipid structure and function

#### BASIC ONCOLOGY:

- 1. Structural features of biologic membranes
- 2. Tumor cell membranes, tumor-associated antigens

#### GRADUATE BIOCHEMISTRY:

- 1. Stereochemistry of carbohydrates
- 2. Conformations of carbohydrates
- 3. Chemical reactivity and conformation
- 4. Methodology for structural determinations of carbohydrate sequences
- 5. Types and characteristics of complex carbohydrates
- 6. Methods applied to analysis of complex carbohydrates
  - 7. Synthesis of complex carbohydrates
  - 8. Functions of complex carbohydrates
  - 9. Proteins primary and secondary structure
  - 10. Proteins Tertiary and quaternary structure
  - 11. Protein-protein and protein-ligand interactions
  - 12. Proteins structural predictions
  - 13. Enzyme kinetics
  - 14. Enzyme mechanisms
  - 15. Enzymes Types and regulation

- 16. Membrane structure and function
- 17. DNA and RNA structures
- 18. Principles that determine polynucleotide structure
- 19. Protein polynucleotide interactions

#### LECTURES, DENTAL BIOCHEMISTRY

- 1. Glycogen metabolism and regulation of blood glucose
- 2. Structure and function of phospholipids, membrane structure
- 3. Fatty acid synthesis and degradation
- 4. Interrelationships and regulation of metabolic pathways

#### IMMUNOCHEMISTRY:

- 1. Heterogeneity of the antibody response; classes, subclasses, allo- and idiotypes of Igs
- 2. Structural features of Igs; discussion of homologies and deduction of structure from amino acid sequence data
- 3. Effector functions of the Iqs
- 4. Three dimensional structure of Igs and quaternary interactions of domains
- 5. Antibody combining site constructs
- 6. Antibody combining site interactions with haptens; serologic specificities
- 7. Measurement, interpretation and quantitations of antibody-antigen interactions
- 8. Kinetic analyses of antibody-hapten interactions
- 9. Radio- and enzyme-immunoassays
- 10. Parameters of antigenicity and immunogenicity

#### CANCER PHARMACOLOGY:

- 1. Progression and selection of tumor cell populations; changes in cell surface composition and interactions with metastases
- 2. Tumor-associated antigens

#### RESIDENT AND STAFF LECTURES:

Otolaryngology: lectures on overview of tumor immunology

Rheumatology:

- Synovial cell metabolism and antigen, genetic analysis of antigen expression
- 2. Protein Polymorphisms: types, effects on protein function, contribution to disease processes

#### Subjects taught in Medical Biochemistry Laboratory:

- 1. Principles and methods of automated analyses
- 2. Acid-base regulation and imbalances
- 3. Statistical methods and analyses of clinical data
- 4. Dietary calculations of protein, carbohydrate, lipid, caloric intake and nitrogen balance
  - 5. Presentations, analysis, critique of primary clinical and basic research papers

#### Current Teaching:

Lectures in graduate biochemistry: Characterizations

proteins, protein secondary, tertiary of quaternary structures, predictions of protein and peptide structures, binding site interactions with various proteins ligands, structures of polynucleotides, chemistry, stereochemistry and conformations of carbohydrates, structural types of carbohydrates, complex carbohydrate biosynthesis, functions of complex carbohydrates.

Lectures in medical and dental biochemistry: on carbohydrate, lipid and phospholipid structure and function, glycogen metabolism and regulation of blood glucose, fatty acid synthesis and degradation, and integration and regulation of carbohydrate and lipid metabolism.

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Feizi, T., Kabat, E.A., Vicari, G., Anderson, R. and Marsh, W.L., "The I Antigen Complex-Precursors in the A, B, Le I and Le Blood Group System, Hemagglutination Inhibition Studies," J. Exp. Med., 133, 39-52, 1971.

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Rovis, L., Anderson, B., Kabat, E.A., Gruezo, F. and Liao, J., "Heterogeneity of Carbohydrate Fragments Isolated from Human Blood Group H and Le Active Glycoproteins by Base-Borohydride Degradation," <u>Biochemistry</u>, <u>12</u>, 1955-1961, 1973.

Rovis, L., Anderson, B., Kabat, E.A., Gruezo, F. and Liao, J., "Structures of Oligosaccharides Produced by Base-Borohydride Degradation of Human H, Le and Le Active Glycoproteins," <u>Biochemistry</u>, 12, 5340-5354, 1973.

Rovis, L., Anderson, B. and Kabat, E.A., "Immunochemical Studies on Blood Group A, B, H, Le and Le and Precursor I Substances," in <a href="Methodologie de la Structure et du">Methodologie de la Structure et du</a>

Metabolism des Glycoconjuges, 645-650, 1974.

#### Enzyme Kinetic Studies

Abstract: Anderson, R. and Czerlinski, G., "Enzyme Amplification for the Detection of Very Low Levels of Substrate Concentration," Biophysical Society, San Francisco, CA, Feb., 1986.

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## Connective Tissue Activating Protein

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Abstract: Weiss, J.J., Sloan, T.B., Castor, C.W. and Anderson, B., "Detection of Platelet-Derived CTAP-III in Biologic Specimens," Mid-West Immunology Conference, 1979.

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## <u>Carbohydrate Sequence Epitopes and Anti-Carbohydrate</u> Specificities

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#### PATENT APPLICATIONS

1. Binding of immune complexes by modified forms of c-reactive protein.

Applicants: Northwestern University and

Rush - Presbyterian - St. Luke's Medical Center

Inventors: Potempa and Anderson

U.S. application Serial No. 07/582,884,

Filed: October 3, 1990

Refiled: 08/271,137; July 6, 1994 - 2545/73

Status: Issued: January 14, 1997; US Letter

Patent No. 5,593,897

PCT application number PCT/US89/01247

Filed March 31, 1989 (2545/11)

Status: Nationalized

Australian application no. 34485/89 Filed: March 31, 1989 (2545/24)

Status: Issued, 6/11/93; Serial #633488

Japanese application No. 1-504716 Filed: March 31, 1989 (2545/26)

Status: Pending, awaiting examination

Canadian application No. 595,543 Filed April 3, 1989 (2545/10) Status: Pending, no action yet

EPO application No. 89904944.9 Filed March 31, 1989 (2545/25)

2. A synthetic peptide and its uses Applicant: Northwestern University

Inventors: Baumann and Anderson

U.S. application Serial No. 07/598,416 Filed: October 16, 1990 (2545/28)

Status: Issued November 15, 1994

Patent Number 5,364,930

PCT application number PCT/US91/07581

Filed: October 9, 1991

Status: Pending

#### PATENT APPLICATIONS - continued

3. Binding of aggregated immunoglobulin or immune complexes by serum amyloid P component Applicant: Northwestern University
Inventors: Anderson and Brown
U.S. application Serial No. 07/672,526

Filed: March 19, 1991 (2545/21) Status: Issued 6/22/93, P-5,221,628

4. Immunoassay for glycosylated proteins employing antibody to reductively glycosylated amino acids

Applicant: Northwestern University

Inventors: Davis and Anderson

U.S. application Serial No. 07/397,781

(2545/5)

08/068,525 (5/27/93) (2545/51) 08/151,073 (11/12/93) (2545/52)

Filed: Augu

August 23, 1989

Status: Granted; U.S. Letters Patent No.

5,484,735

PCT application no. PCT/US90/04666 Filed: August 17, 1990 (2545/23)

Status: Nationalized

EPO application no. 90913261.5

Filed: August 17, 1990 (2545/37)

Status: Granted

Japanese application no. 2-512516

Filed: August 17, 1990 (2545/38)

Status: Pending, awaiting examination

# PATENT APPLICATIONS - continued

5. Immunoassay for detecting and monitoring alcoholics Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Makhlouf, Pankow, Anderson and Bean

U.S. application Serial No. 07/765,169;

Filed: September 25, 1991 (2545/8)

08/272,852; July 08, 1994 (2545/74)

Status: granted

PCT application Serial No. PCT/US92/08136 Filed: September 25, 1992 (2545/44)

Status: Nationalized

EPO application no. 92921176.1

Filed: August 25, 1992 (2545/60), granted

Japanese application no. 5-506376

Filed: 9/25/92 (2545/61)

Canadian application no. 2119651 Filed: 9/25/92 (2545/59), granted

Australian application no. 27577/92 Filed 9/23/92 (2545/58), granted

6. Methods of Treating Cancer Using Modified C-Reactive Protein

Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Potempa, Kresl and Anderson

U.S. application Serial No. 07/874,263

Filed: April 24, 1992

Status: Issued December 12, 1995

US Letters Patent No. 5,474,904

PCT application no. PCT/US/03769

Filed:

4/22/92 (2545/50)

Status:

Nationalized

EPO application no. 93910710.8, Filed: 4/22/93 (2545/81)

Japanese application no.5-518361, Filed: 4/22/93 (2545/80)

Canadian application no. 2432001, Filed: 4/22/93 (2545/80)

Australian application no. 41109/93, Filed: 4/22/93 (2545/79)

#### PATENT APPLICATIONS - continued

7. Method of detecting cancer

Applicants: Northwestern University and Immtech Int.

Inc.

Inventors: Anderson and Davis

U.S. application Serial No. 07/939,830

Filed: September 3, 1992 (2545/9) Status:

Issued December 27, 1994

Patent Number 5,376,531

Japanese application No. 4-293052

Filed: October 30, 1992 (2545/45)

Status: Pending

8. Methods of Imaging Cancer Cells Using Modified C-

Reactive Protein

Applicant: Northwestern University

Inventors: Potempa, Kresl and Anderson

U.S. Application 149,663

Filed Nov. 9, 1993

Status: Issued December 12, 1995

US Letters Patent No. 5,474,904

CIP to Synthetic Clq Peptide Fragments - use 9.

transplantation

Applicant: Northwestern University

Inventors: Baumann, Anderson and Fryer

Filed: April 6, 1996 to US patent office

Status: granted

PCT of same:

Application and Inventors: Baumann, Anderson and Fryer

Filed: April 4, 1997

Status: withdrawn

10. Method of Inhibiting Complement

Applicants and Inventors: Anderson and Fryer

April 14, 1997 to US patent office Filed:

Status: granted

11. Peptides Comprising Aromatic D-Amino Acids and Methods

Of Use

Inventor: Byron E. Anderson

US patent filed July 3, 2002

PCT application filed July 3, 2003